be formed by that analyte when it resides on the surface of the fluid. The total surface area of the fluid increases as the number of Taylor cones at the nozzle tip increases resulting in the increase in solution phase ions at the surface of the fluid prior to electrospray formation. The ion intensity will increase as measured by the mass spectrometer when the number of electrospray plumes increase as shown in the example above.

[0147] Another important feature of the present invention is that since the electric field around each nozzle is preferably defined by the fluid and substrate voltage at the nozzle tip, multiple nozzles can be located in close proximity, on the order of tens of microns. This novel feature of the present invention allows for the formation of multiple electrospray plumes from multiple nozzles of a single fluid stream thus greatly increasing the electrospray sensitivity available for microchip-based electrospray devices. Multiple nozzles of an electrospray device in fluid communication with one another not only improve sensitivity but also increase the flow rate capabilities of the device. For example, the flow rate of a single fluid stream through one nozzle having the dimensions of a 10 micron inner diameter, 20 micron outer diameter, and a 50 micron length is about 1 μL/min.; and the flow rate through **200** of such nozzles is about 200 μL/min. Accordingly, devices can be fabricated having the capacity for flow rates up to about 2 μL/min., from about 2 μL/min. to about 1 mL/min., from about 100 nL/min. to about 500 nL/min., and greater than about 2 μL/min. possible.

[0148] Arrays of multiple electrospray devices having any nozzle number and format may be fabricated according to the present invention. The electrospray devices can be positioned to form from a low-density array to a high-density array of devices. Arrays can be provided having a spacing between adjacent devices of 9 mm, 4.5 mm, 2.25 mm, 1.12 mm, 0.56 mm, 0.28 mm, and smaller to a spacing as close as about 50 μm apart, respectively, which correspond to spacing used in commercial instrumentation for liquid handling or accepting samples from electrospray systems. Similarly, systems of electrospray devices can be fabricated in an array having a device density exceeding about 5 devices/cm^2, exceeding about 16 devices/cm^2, exceeding about 30 devices/cm^2, and exceeding about 81 devices/cm^2, preferably from about 30 devices/cm^2 to about 100 devices/cm^2.

[0149] Dimensions of the electrospray device can be determined according to various factors such as the specific application, the layout design as well as the upstream and/or downstream device to which the electrospray device is interfaced or integrated. Further, the dimensions of the channel and nozzle may be optimized for the desired flow rate of the fluid sample. The use of reactive-ion etching techniques allows for the reproducible and cost effective production of small diameter nozzles, for example, a 2 μm inner diameter and 5 μm outer diameter. Such nozzles can be fabricated as close as 20 μm apart, providing a density of up to about 160,000 nozzles/cm^2. Nozzle densities up to about 10,000/cm^2, up to about 15,625/cm^2, up to about 27,566/cm^2, and up to about 40,000/cm^2, respectively, can be provided within an electrospay device. Similarly, nozzles can be provided wherein the spacing on the ejection surface between the centers of adjacent exit orifices of the spray units is less than about 500 μm, less than about 200 μm, less than about 100 μm, and less than about 50 μm, respectively. For example, an electrospray device having one nozzle with an outer diameter of 20 μm would respectively have a surrounding sample well 30 μm wide. A densely packed array of such nozzles could be spaced as close as 50 μm apart as measured from the nozzle center.

[0150] In one currently preferred embodiment, the silicon substrate of the electrospray device is approximately 250-500 μm in thickness and the cross-sectional area of the through-substrate channel is less than approximately 2,500 μm^2. Where the channel has a circular cross-sectional shape, the channel and the nozzle have an inner diameter of up to 50 μm, more preferably up to 30 μm; the nozzle has an outer diameter of up to 60 μm, more preferably up to 40 μm; and nozzle has a height of (and the annular region has a depth of) up to 100 μm. The recessed portion preferably extends up to 300 [μm outwardly from the nozzle. The silicon dioxide layer has a thickness of approximately 1-4 μm, preferably 1-3 μm. The silicon nitride layer has a thickness of approximately less than 2 1m.

[0151] Furthermore, the electrospray device may be operated to produce larger, minimally-charged droplets. This is accomplished by decreasing the electric field at the nozzle exit to a value less than that required to generate an electrospray of a given fluid. Adjusting the ratio of the potential voltage of the fluid and the potential voltage of the substrate controls the electric field. A fluid to substrate potential voltage ratio approximately less than 2 is preferred for droplet formation. The droplet diameter in this mode of operation is controlled by the fluid surface tension, applied voltages and distance to a droplet receiving well or plate. This mode of operation is ideally suited for conveyance and/or apportionment of a multiplicity of discrete amounts of fluids, and may find use in such devices as ink jet printers and equipment and instruments requiring controlled distribution of fluids.

[0152] The electrospray device of the present invention includes a silicon substrate material defining a channel through the substrate between an entrance orifice on a reservoir surface and a nozzle on a nozzle surface such that the electrospray generated by the device is generally perpendicular to the nozzle surface. The nozzle has an inner and an outer diameter and is defined by an annular portion recessed from the surface. The recessed annular region extends radially from the nozzle outer diameter. The tip of the nozzle is co-planar or level with and preferably does not extend beyond the substrate surface. In this manner the nozzle can be protected against accidental breakage. The nozzle, channel, reservoir and the recessed annular region are etched from the silicon substrate by reactive-ion etching and other standard semiconductor processing techniques.

[0153] All surfaces of the silicon substrate preferably have insulating layers to electrically isolate the liquid sample from the substrate such that different potential voltages may be individually applied to the substrate and the liquid sample. The insulating layers can constitute a silicon dioxide layer combined with a silicon nitride layer. The silicon nitride layer provides a moisture barrier against water and ions from penetrating through to the substrate causing electrical breakdown between a fluid moving in the channel and the substrate. The electrospray apparatus preferably includes at least one controlling electrode electrically contacting the substrate for the application of an electric potential to the substrate.